Quarterly Surveillance Report

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Thyroid Cancer

Thyroid cancer is rare. It accounts for 1% of all incident (newly diagnosed) cancers in the US. In Montana, thyroid cancer accounts for 2% of all incident cancers and substantially less than 1% of all cancer deaths. There are several subtypes of thyroid cancer. The most common arise from the epithelium as papillary (80%) or follicular (15%) tumors. Other rare types, including anaplastic and medullary carcinomas, account for the remaining 5%. Each type has different risk factors.

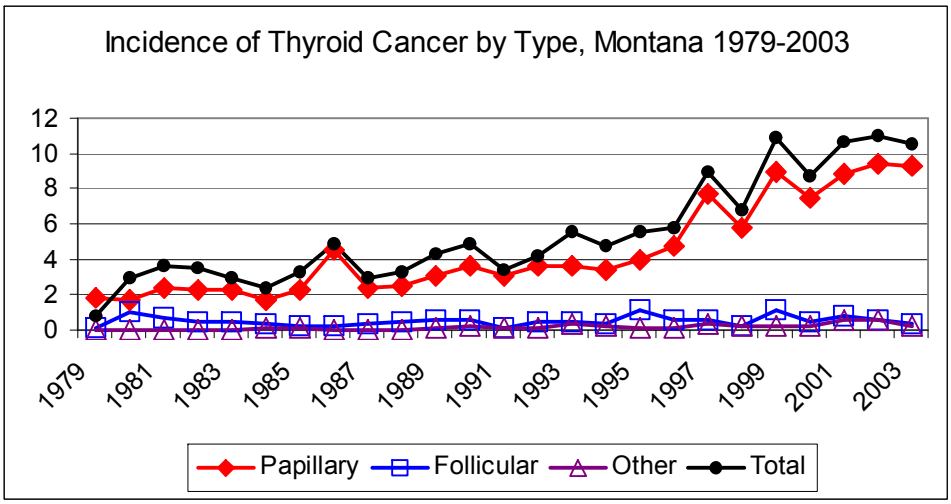
Risk Factors for Thyroid Cancer

Papillary cancer has an approximately equal sex ratio in children. The incidence among women increases dramatically at puberty so the sex ratio is 3:1 during the reproductive years, followed by a return to nearly 1:1 among the elderly. Investigations of possible hormonal and reproductive risk factors have been inconsistent. Investigations of dietary, occupational, and environmental exposures have also been inconsistent, with the exception of iodine intake and exposure to radiation. Risk factors for rare types of thyroid cancer are difficult to study. Many appear to have a genetic component. Half of all patients diagnosed with thyroid cancer of any type have no known risk factors.

The relationship between thyroid cancer and iodine intake is complex. Iodine deficiency and goiter are associated with increased risk of follicular cancer. In the absence of exposure to radiation, chronic iodine excess is associated with increased risk of papillary cancer. Radiation of all kinds increases the risk of papillary cancer. Exposure to radioactive iodine (I-131) is a special risk factor and iodine deficiency is associated with increased risk of papillary cancer in the presence of I-131 because the thyroid gland absorbs iodine avidly in the deficient state, resulting in absorption of I-131. Iodine supplementation is the recommended short-term prophylactic treatment for acute exposure to I-131.

Trends in Thyroid Cancer Incidence

The incidence of papillary thyroid cancer has been increasing in Montana since the late 1980's. Follicular and other rare types have been constant at a very low incidence (less than 1 per 100,000 per year on average) for the past 25 years. Because papillary histology accounts for approximately 80% of all thyroid cancer, the incidence curve for total thyroid cancer closely parallels that for papillary cancer.



The increasing incidence of papillary thyroid cancer in Montana is not unique. Incidence has been increasing in developed countries around the world: by an average of 3% per year in the US between 1973 and 2002; by 6% to 8% per year in France between 1980 and 2000; and by 1% per year in Scotland between 1960 and 2002.[1] Does this reflect a true increase in incidence, or is it an artifact of such trends as better diagnosis, aging populations, or the discovery of asymptomatic tumors at autopsy?

Radiation Exposure

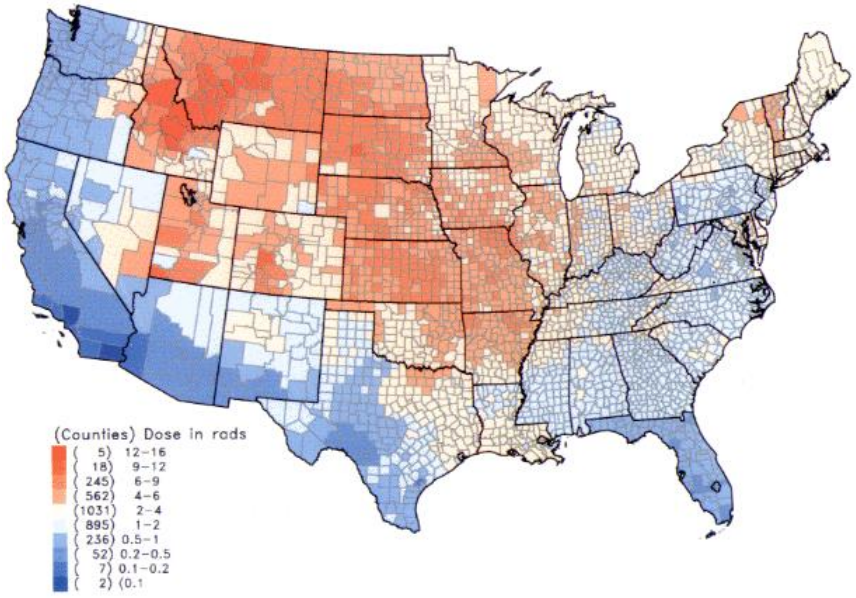
Radiation exposure, especially in childhood, is the greatest risk factor for papillary thyroid cancer. The main sources of exposure are therapeutic radiation treatments and environmental exposure to I-131 from atmospheric nuclear testing. Therapeutic radiation to the head, neck, and chest was used from the 1940s through the early 1960s to treat such childhood ailments as acne, otitis media, tinia capitis, tonsillar hypertrophy, thymic enlargement, and asthma. Up to 9% of children who received these treatments developed papillary thyroid cancer with a latency of 20 years or more. On a population basis, the number of children exposed in this way is likely to be relatively small.

The greatest potential population-wide risk factor for papillary thyroid cancer is atmospheric nuclear testing that occurred worldwide between 1940 and 1980. Atmospheric testing released several radioactive isotopes but only I-131 increases the risk of thyroid cancer. By far the largest contribution to risk for residents of Montana and the United States as a whole was the Nevada Test Site, 65 miles north of Las Vegas. It was in operation until 1970 but 99% of its I-131 was released between 1952 and 1957. It is apparent from the map on the next page, created by the National Cancer Institute (NCI), that Montana residents had very high potential exposure to I-131 from the Nevada Test

[1] Hodgson et al., 2004, *Ann Surg Oncol* 11:1093-1097; Leenhardt et al., 2004, *Thyroid* 14:1056-1060; Reynolds et al., 2005, *Clin Endocrinol* 62:156-162.

Site. Although the Hanford Nuclear Reservation in Washington is closer to Montana, extensive investigations have not documented any I-131 reaching Montana from Hanford.[2]

Estimated Per Capita Cumulative Dose of I-131
Nevada Test Site Above-Ground Tests[3]



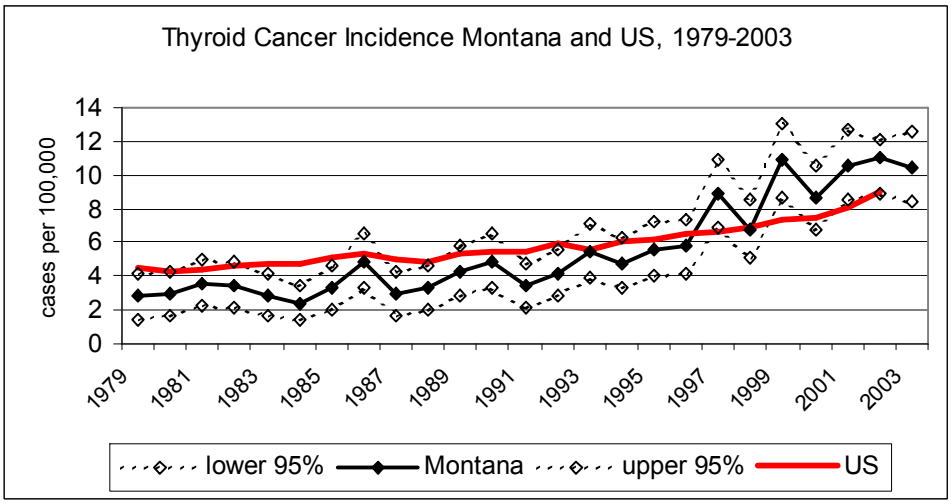
There have been many studies of acute and long-term effects of I-131 exposure among Japanese atom bomb survivors in World War II, Marshall Island residents downwind from early atmospheric testing at Bikini Atoll, and residents near nuclear reactor accidents, notably the massive Chernobyl disaster in 1986. The largest study was an exhaustive investigation mandated by Congress and conducted by the NCI, evaluating exposure among US residents as a result of activities at the Nevada Test Site.[4] All studies suggest that a real increase in papillary thyroid cancer was to be expected in the US between 1960 and 2000.

The risk incurred from exposure to I-131 depends on age, diet, distance from the source of radiation, geography, and weather conditions at the time of release.[5] People who were under the age of 10 between 1945 and 1962 are at the greatest risk. The path of exposure was I-131 falling to earth in rain onto pasture grass, where cows and other animals consumed the grass and I-131. The primary source of exposure for children was drinking milk, especially goat's milk, which concentrates I-131 10 times more effectively than cow's milk.

[2] http://www.doh.wa.gov/hanford/resources/studies.html
[3] http://rex.nci.nih.gov/massmedia/exesumfig1.html
[4] http://rex.nci.nih.gov/massmedia/Fallout/index.html
[5] http://www.atsdr.cdc.gov/HEC/CSEM/iodine/docs/iodine131.pdf

Fortunately, half of the radioactivity from I-131 dissipates within 8 days (its half-life). Just 2% remains after 60 days and it is no longer measurable after a year. Only direct exposure to atmospheric fallout (comparatively rare), or prompt consumption of milk from animals pastured outside immediately after a release increase risk. Increased incidence is not apparent for 20 years or more after exposure, the latency period for developing papillary thyroid cancer.

Based on the NCI's "I-131 Thyroid Dose/Risk Calculator for NTS Fallout,"[6] people who grew up in Montana in the 1940s through 1960s are projected to have as much as a seven-fold increase in thyroid cancer risk. Fortunately, incidence rates for Montana do not support this projection. The graph below shows the incidence rates for Montana and the 95% Confidence Intervals (CI) around those rates, reflecting the statistical uncertainty of rates calculated from small numbers of cases. If the CI encompassed by the dotted lines does not include the red line of the national rate, the Montana rate is significantly different than the national rate. If the CI includes the red line, the Montana rate is not significantly different than the national rate. Montana's incidence was lower than the national incidence in eight years between 1979 and 1992; it was higher than the national incidence only in 1997, 1999, and 2001. It is too soon to tell if the recent increase over the national rate in Montana is a robust trend or merely fluctuations in estimates for a rare cancer in a relatively small population.



The Public Health Approach to Thyroid Cancer

The public health approach to cancer focuses on prevention and early detection. I-131 exposure is the most important risk factor for thyroid cancer. Even though nuclear testing ceased 30 years ago, many residents of the US, especially in Montana, Idaho, and

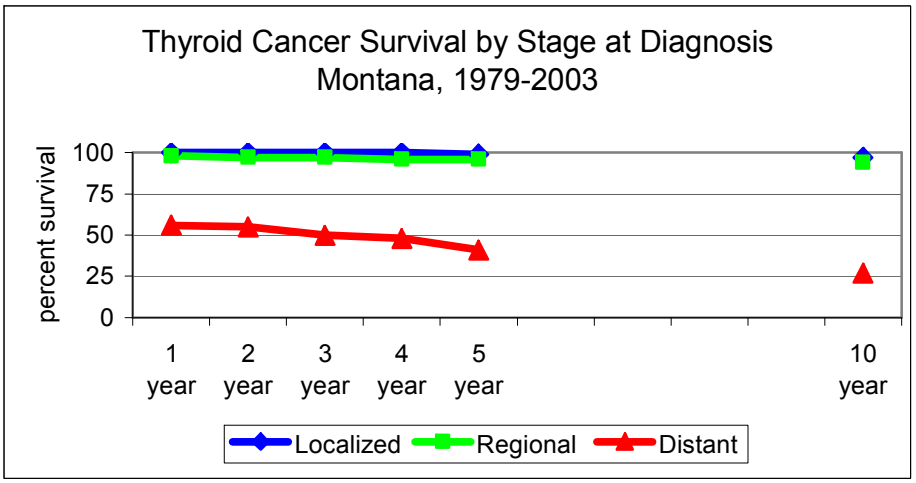
[6] http://ntsi131.nci.nih.gov/

the Midwest, remain at increased risk of developing papillary thyroid cancer because of exposure to I-131 in childhood. The highest risk applies to individuals born between 1935 and 1962 and living in the most severely affected states for the first 10 years of life, and to individuals who received therapeutic radiation to the head and neck in childhood.

Although the population at risk is potentially large, screening for thyroid cancer is not recommended because there is no sensitive (does not miss true cases) and specific (few false positives) screening test for thyroid cancer.[7] Thyroid cancer most often presents with palpable nodules, occasionally with hoarseness, difficulty swallowing, or localized pain. Thyroid tumors are sometimes associated with altered concentrations of thyroid hormones in the blood. None of these are specific for thyroid cancer and all are more often caused by other conditions. Thyroid nodules occur in 7% of women and 2% of men in the US. Approximately 2% of nodules are cancerous; nodules are more likely to be cancerous in men, children, and the elderly.

Early Detection and Survival

Most thyroid cancers are detected during routine physical examinations because clinicians are alert for signs of thyroid disease. Clinicians should be especially suspicious of thyroid cancer in patients with a history of radiation exposure. Survival is excellent if thyroid cancer is diagnosed early. Over the past 25 years, most incident thyroid cancers have been diagnosed at a localized (68%) or regional (27%) stage in Montana; only 5% have been classified as distant at diagnosis. Patients diagnosed at localized or regional stages have nearly 100% survival at 5 years after diagnosis and approximately 95% survival at 10 years. In contrast, nearly half of patients diagnosed with metastatic thyroid cancer do not survive a year after diagnosis and only a quarter survive for 10 years.



[7] US Preventive Services Task Force, www.ahrq.gov/clinic/2ndcps/thyrcan.pdf

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